

**AMENDMENT**

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

**IN THE CLAIMS:**

Kindly amend the claims, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, to read as follows:

1-39. (Cancelled)

40. (New) A method of identifying a modulator of a  $\beta 3$  sub-unit polypeptide, the method comprising the steps of: (a) providing a  $\beta 3$  sub-unit polypeptide; (b) contacting the  $\beta 3$  sub-unit polypeptide with a candidate molecule; and (c) detecting binding between the candidate molecule and the  $\beta 3$  sub-unit polypeptide, in which the  $\beta 3$  sub-unit polypeptide has at least 80% amino acid identity with the amino acid sequence of SEQ ID NO 2 over the entire length of the sequence of SEQ ID NO 2, or with a peptide fragment thereof, said  $\beta 3$  sub-unit polypeptide being capable of co-operating with at least one  $\alpha$ -subunit of voltage-gated sodium channels to form an active sodium channel.

41. (New) A method according to Claim 40, in which the  $\beta 3$  sub-unit polypeptide is part of an intact cell or a membrane preparation.

42. (New) A method according to Claim 40, in which binding between the candidate molecule and the  $\beta 3$  sub-unit polypeptide is detected by a method selected from the group consisting of: chromatography, mass spectroscopy, Biacore and Fluorescence Energy Transfer (FRET).

43. (New) A method according to Claim 40, in which the method further comprises detecting modulation of activity of the  $\beta 3$  sub-unit polypeptide by the candidate molecule.

44. (New) A method according to Claim 40, in which the candidate molecule induces a change in the activation potential, the inactivation time, or the rate of recovery of a sodium channel comprising the  $\beta 3$  sub-unit polypeptide.

45. (New) A method according to Claim 40, in which the candidate molecule induces any one or more of the following: a decrease in the inactivation potential, a decrease in the rate

of inactivation or a decrease in the rate of recovery from inactivation of a sodium channel comprising the  $\beta 3$  sub-unit polypeptide.

46. (New) A method according to Claim 40, in which the candidate molecule is selected from the group consisting of: a peptide, a protein, an antibody and a chemical entity.

47. (New) A method according to Claim 40, in which the candidate molecule is selected from the group consisting of: voltage-dependent channel blockers, tetrodotoxin, lidocaine, phenytoin, carbamazepine, lamotrigine, zonisamide, riluzole, lifarizine, ralitoline, flunarizine, verapamil and carvedilol, a molecule from the phenylacetamide family, 6-Iodoamiloride, a sodium channel opener, carsatrin or BDF-9148 (Beiersdorf), a therapeutic molecule active on neuropathic pain or migraine and CNS-5161 (Cambridge Neuroscience).

48. (New) A method for screening ligand substances or molecules that modulate the biological activity of a voltage-gated sodium channel containing a  $\beta 3$  sub-unit polypeptide, said method comprising: (a) contacting the ligand with the  $\beta 3$  sub-unit polypeptide; (b) contacting the ligand and the  $\beta 3$  sub-unit polypeptide with a  $\beta 3$  substrate and allowing binding of the substrate to the  $\beta 3$  sub-unit polypeptide to occur; and (c) measuring binding of the substrate to the  $\beta 3$  polypeptide, in which the  $\beta 3$  sub-unit polypeptide has at least 80% amino acid identity with the amino acid sequence of SEQ ID NO 2 over the entire length of the sequence of SEQ ID NO 2, or with a peptide fragment thereof, said  $\beta 3$  sub-unit polypeptide being capable of cooperating with at least one  $\alpha$ -subunit of voltage-gated sodium channels to form an active sodium channel.

49. (New) A method for screening ligand substances or molecules that modulate the biological activity of a voltage-gated sodium channel containing a  $\beta 3$  sub-unit polypeptide, said method comprising: (a) obtaining a recombinant host cell coexpressing a  $\beta 3$  sub-unit polypeptide and a functional  $\alpha$  sub-unit, preferably an  $\alpha 2$  sub-unit of a voltage-gated sodium channel; (b) bringing into contact said recombinant host cell with a substance or molecule to be tested; and (c) measuring an electrical parameter, in which the  $\beta 3$  sub-unit polypeptide has at least 80% amino acid identity with the amino acid sequence of SEQ ID NO 2 over the entire length of the sequence of SEQ ID NO 2, or with a peptide fragment thereof, said  $\beta 3$  sub-unit polypeptide being capable of co-operating with at least one  $\alpha$ -subunit of voltage-gated sodium channels to form an active sodium channel.

50. (New) A method according to Claim 49, in which the electrical parameter is measured by a voltage clamp technique.
51. (New) A method according to Claim 49, in which the electrical parameter comprises membrane potential measured by a voltage sensitive fluorescent dye.
52. (New) A method according to Claim 49, in which the electrical parameter to be measured comprises inactivation potential.
53. (New) A method according to Claim 49, in which the electrical parameter to be measured comprises inactivation time.
54. (New) A method according to Claim 49, in which the electrical parameter to be measured comprises the rate of recovery of the sodium channel.
55. (New) A method for screening ligand substances or molecules which modulate the biological activity of a voltage-gated sodium channel containing a  $\beta 3$  sub-unit polypeptide, said method comprising: (a) obtaining a recombinant host cell coexpressing a  $\beta 3$  sub-unit polypeptide and a functional  $\alpha$  sub-unit, preferably an  $\alpha 2$  sub-unit of a voltage-gated sodium channel; (b) bringing into contact said recombinant host cell with a substance or molecule to be tested; and (c) measuring a change in sodium flux, in which the  $\beta 3$  sub-unit polypeptide has at least 80% amino acid identity with the amino acid sequence of SEQ ID NO 2 over the entire length of the sequence of SEQ ID NO 2, or with a peptide fragment thereof, said  $\beta 3$  sub-unit polypeptide being capable of co-operating with at least one  $\alpha$ -subunit of voltage-gated sodium channels to form an active sodium channel.
56. (New) A method according to Claim 55, in which the change in sodium flux is measured through a sodium flux measuring technique by sodium sensitive dyes such as SBFI.
57. (New) A method according to Claim 55, in which the parameter to be measured comprises an increase in sodium concentration within the cell.
58. (New) A method according to Claim 55, in which the parameter to be measured comprises a decrease in sodium concentration within the cell.
59. (New) A method according to Claim 55, in which the parameter to be measured comprises the rate of recovery of the sodium channel.
60. (New) A method according to Claim 40 for identifying a molecule suitable for the treatment or alleviation of pain, epilepsy, febrile seizures, generalised epilepsy, stroke,

ischemia, heart disease, Jacobsen Syndrome, Familial Nonchromaffin Paraganglioma, Phenylketonuria due to PTS deficiency or Charcot Marie Tooth disease.

61. (New) A method of treating or alleviating pain, epilepsy, febrile seizures, generalised epilepsy, stroke, ischemia, heart disease, Jacobsen Syndrome, Familial Nonchromaffin Paraganglioma, Phenylketonuria due to PTS deficiency or Charcot Marie Tooth disease comprising administration of a modulator of a  $\beta 3$  sub-unit polypeptide to a subject in need thereof.